Remarks

Claims 1-26 were pending. By way of this response, claims 1 and 25 have been amended. Support for the amendments to the specification and the claims can be found in the application as originally filed, and no new matter has been added. In addition, applicant respectfully submits that the amendments to the claims do not raise new issues, and applicant respectfully requests entry of this Amendment and reconsideration of the rejections.

Accordingly, claims 1-26 remain pending.

Claims 7-10, 13-15, and 17-21 remain withdrawn from consideration. Applicant respectfully submits that claim 1 is generic to these withdrawn claims, and respectfully requests that claims 7-10, 13-15, and 17-21 be examined and found allowable upon indication of the allowability of claim 1.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 11, 12, 16, and 22-26 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor(s) had possession of the claimed invention. In particular, the Office Action indicates that the specification does not include a description with regard to the cause of hyperlipidemia.

Applicant has amended claims 1 and 25, as set forth above. Applicant respectfully traverses the rejections as they relate to the amended claims.

Claims 1 and 25 have been amended by replacing the language regarding a cause of hyperlipidemia with language reflecting that retinoids are not coadministered to the mammal with the RAR antagonist or inverse agonist when treating hyperlipidemia. The amendments to claims 1 and 25 similarly apply to the claims dependent therefrom.

As acknowledged in the Office Action (page 3, 2nd full paragraph), applicant submits that the specification clearly and sufficiently describes the claimed invention. In particular, the specification contains a clear description that the presently claimed methods are practiced without coadministering retinoids with RAR antagonists or inverse agonists. As indicated in applicant's previous responses, Klein (U.S. Pat. No. 5,776,699) was incorporated by reference into the present application (e.g., see page 6, lines 15-18). Among other things, Klein may be relied upon for its disclosure and teachings of coadministration of retinoids and RAR antagonists or inverse agonists to a patient. In addition, Klein may be relied on for its disclosure of the antagonistic effects mediated by RAR antagonists or inverse agonists with respect to retinoids (see Example 4, Table I). In addition, the instant application discloses therapeutic effects of RAR antagonists and inverse agonists when they are administered to a patient by themselves or without other pharmaceutically active agents. In other words, the RAR antagonists and inverse agonists disclosed

in the instant application are administered to a subject without the coadministration of retinoids, as disclosed in Klein.

In view of the above, applicant submits that the present claims are properly described in the specification to satisfy the requirements of 35 U.S.C. § 112.

Rejections Under 35 U.S.C. § 103

Claims 1-6, 11, 12, 16, and 22-26 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Klein (U.S. Pat. No. 5,776,699) in view of Aberg (Atherosclerosis, 1985), both of which are of record. The Examiner contends that one of ordinary skill in the art would be motivated to employ 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thichromen-6-yl]-ethynyl]-benzoic acid in a method of lowering triglyceride and preventing myocardial infarction because the RAR antagonists of Klein et al. are known to be useful in inhibiting hypertriglyceridemia.

Applicant respectfully traverses the rejection. As indicated in applicant's previous response, Klein states that the compounds disclosed therein "can block hypertriglyceridemia caused by coadministered retinoids" (column 20, line 65 to column 21, line 1). Klein does not specifically teach or suggest the use of RAR antagonists or inverse agonists to treat naturally occurring hyperlipidemia. In addition, as indicated earlier, Klein discloses preventing increases in triglyceride levels caused by coadministration of retinoids (see Example 4, Table 10). Klein does not specifically disclose or suggest that RAR antagonists or inverse agonists reduce lipid levels in patients who were not coadministered retinoids, as recited in

the present claims. Thus, Klein alone, or in combination with Aberg, does not specifically teach or suggest treating hyperlipidemia as recited in the pending claims.

Because Klein does not specifically teach or suggest the present invention of treating hyperlipidemia without coadministering retinoids, as recited in the claims, one or ordinary skill in the art would not be motivated by Klein to use RAR antagonists, including AGN 194310, to treat hyperlipidemia as claimed, let alone be motivated to combine the teachings of Klein with those of Aberg to prevent myocardial infarction. Among other things, methods of preventing increases in triglyceride levels caused by retinoids using a RAR antagonist or inverse agonist may occur by entirely different mechanisms than reducing lipid levels in patients that have not been coadministered retinoids. Thus, applicant submits that there would be no reasonable expectation of success to use the agents disclosed by Klein to treat hyperlipidemia in patients who were not coadministered retinoids, and thus, one of ordinary skill in the art would not be motivated to use RAR antagonists or inverse agonists as recited in the pending claims.

However, even if a motivation were present to combine the disclosure of Klein with Aberg, which applicant does not concede, the combination would fail to teach or suggest all of the claimed limitations in the present claims. As discussed above, the present claims are directed to methods of treating hyperlipidemia in a mammal by administering a RAR antagonist or inverse agonist without coadministering a retinoid to the mammal. Klein discloses preventing increases in trigylcerides caused by coadministration of retinoids. Thus, because all of

the claim limitations recited in the present claims are not specifically disclosed or suggested by the combination of Klein and Aberg, the combination of references fails to make obvious the presently claimed invention.

In addition, regarding the Examiner's indication that the "new matter" limitations have not been examined on the merits (Office Action, page 6), applicant submits that even limitations that do not find support in the original specification must be considered and given weight when evaluating claims for obviousness under 35 U.S.C. § 103 (see MPEP § 2143.03 citing *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983) aff'd mem. 738 F.2d 453 (Fed. Cir. 1984)).

Thus, applicant respectfully requests the Examiner to evaluate the present claims for obviousness based on all of the recited limitations. If the Examiner believes the claims are not deemed to be in condition for allowance, applicant respectfully requests the issuance of a non-final action since all of the claimed limitations have not been considered in issuing the June 2, 2003 and July 16, 2002 Office Actions.

In view of the above, Applicant respectfully submits that claims 1-6, 11, 12, and 22-26 are unobvious and patentable over Klein in view of Aberg under 35 U.S.C. § 103.

In addition, applicant submits that each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods including the additional feature or features recited in any of the present dependent claims.

Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1-26 are allowable. Therefore, applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: July 31/2003

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